

(12) INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(19) World Intellectual Property Organization
International Bureau



(43) International Publication Date
7 November 2002 (07.11.2002)

PCT

(10) International Publication Number
WO 02/087596 A3

(51) International Patent Classification: **A61K 31/7048**,
A61P 1/00, 11/00, 17/00, 29/00, 37/00

(74) Agents: **SCHRELL, Andreas** et al.; Maybachstrasse 6A,
70469 Stuttgart (DE).

(21) International Application Number: **PCT/EP02/03984**

(81) Designated States (*national*): AU, BA, BG, BR, CA, CH,
CN, CZ, HR, HU, ID, IL, IN, JP, MK, MX, NZ, PL, RO,
SI, SK, US, YU, ZA.

(22) International Filing Date: 10 April 2002 (10.04.2002)

(25) Filing Language: English

(84) Designated States (*regional*): Eurasian patent (AM, AZ,
BY, KG, KZ, MD, RU, TJ, TM), European patent (AT, BE,
CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC,
NL, PT, SE, TR).

(26) Publication Language: English

(30) Priority Data:
P010301A 27 April 2001 (27.04.2001) HR

Published:

- with international search report
- before the expiration of the time limit for amending the
claims and to be republished in the event of receipt of
amendments

(71) Applicant (*for all designated States except US*): **PLIVA**
d.d. [HR/HR]; Ulica grada Vukovara 49, 10000 Zagreb
(HR).

(88) Date of publication of the international search report:
3 January 2003

(72) Inventors; and

(75) Inventors/Applicants (*for US only*): **CULIC, Ogn-**
jen [HR/HR]; Medvedgradska 70, 10000 Zagreb (HR).
PARNHAM, Michael [GB/HR]; Licka 33, 10000 Zagreb
(HR). **ERAKOVIC, Vesna** [HR/HR]; Lipa 40a, 51000
Rijeka (HR).

*For two-letter codes and other abbreviations, refer to the "Guid-
ance Notes on Codes and Abbreviations" appearing at the begin-
ning of each regular issue of the PCT Gazette.*

(54) Title: **USE OF AZITHROMYCIN FOR THE MANUFACTURE OF A MEDICAMENT FOR TREATMENT OF NON-IN-
FECTIVE INFLAMMATORY DISEASES**

(57) Abstract: The invention relates to the use of 9-deoxo-9-dihydro-9a-methyl-9a-aza-9a-homoerythromycin. A (generic name: azithromycin) for the therapy of neutrophil-dominated non-infective inflammatory diseases, pharmaceutical compositions containing azithromycin for enteral or parenteral administration and methods for the production of these pharmaceutical compositions.

WO 02/087596 A3

INTERNATIONAL SEARCH REPORT

In tional Application No
PCT/EP 02/03984

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A61K31/7048 A61P1/00 A61P11/00 A61P17/00 A61P29/00
A61P37/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61K A61P

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, EPO-Internal, PAJ, BIOSIS, PASCAL, EMBASE, MEDLINE

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>RUBIN B.K. ET AL: "Macrolide antibiotics as biological response modifiers." CURRENT OPINION IN INVESTIGATIONAL DRUGS, (2000) 1/2 (169-172). , XP001104803 abstract page 169, column 2, paragraphs 2,3,5 page 170, column 1, paragraphs 2,3 page 170, column 2, paragraph 3 page 171, column 1, paragraph 4 --- -/--</p>	<p>1-6, 43-45, 54-56</p>



Further documents are listed in the continuation of box C.



Patent family members are listed in annex.

* Special categories of cited documents :

A document defining the general state of the art which is not considered to be of particular relevance

E earlier document but published on or after the international filing date

L document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

O document referring to an oral disclosure, use, exhibition or other means

P document published prior to the international filing date but later than the priority date claimed

T later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

X document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone

Y document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

G document member of the same patent family

Date of the actual completion of the international search

19 September 2002

Date of mailing of the international search report

29/10/2002

Name and mailing address of the ISA

European Patent Office, P.B. 5818 Patentlaan 2
NL - 2280 HV Rijswijk
Tel. (+31-70) 340-2040, Tx. 31 651 epo nl,
Fax: (+31-70) 340-3016

Authorized officer

Hornich, E

INTERNATIONAL SEARCH REPORT

 International Application No
 PCT/EP 02/03984

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	NARITA NOBUHIRO: "Multi-effect" macrolides." INTERNAL MEDICINE (TOKYO), vol. 39, no. 8, August 2000 (2000-08), pages 599-600, XP001104921 ISSN: 0918-2918 page 599, left-hand column, paragraph 1 page 599, right-hand column, line 4,5	1,2,21, 45,54
X	SCAGLIONE F ET AL: "Comparative anti-inflammatory effects of roxithromycin, azithromycin and clarithromycin." JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY, vol. 41, no. SUPPL. B, March 1998 (1998-03), pages 47-50, XP001104919 ISSN: 0305-7453 abstract page 47, left-hand column, paragraphs 1,2 'Discussion'	1,2,45, 54
X	LABRO M.T. ET AL: "Immunomodulation by macrolide antibiotics." JOURNAL OF CHEMOTHERAPY, (2001) 13/1 (3-8). XP001104982 abstract 'Introduction' page 4, right-hand column figure 2 page 5, right-hand column, paragraph 1 page 7, right-hand column, line 17 - line 25	1-4,6, 45,54
X	DATABASE MEDLINE 'Online! December 2000 (2000-12) GÓMEZ J ET AL: "Prospective, comparative study (1994-1998) of the influence of short-term prophylactic treatment with azithromycin on patients with advanced COPD!" Database accession no. NLM11498704 XP002213965 abstract & REVISTA ESPANOLA DE QUIMIOTERAPIA: PUBLICACION OFICIAL DE LA SOCIEDAD ESPANOLA DE QUIMIOTERAPIA. SPAIN DEC 2000, vol. 13, no. 4, December 2000 (2000-12), pages 379-383, ISSN: 0214-3429	1,2, 21-25, 45,54

INTERNATIONAL SEARCH REPORT

In tional Application No
PCT/EP 02/03984

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>ALTSCHULER E.L.: "Azithromycin, the multidrug-resistant protein, and cystic fibrosis '4!'" LANCET, (25 APR 1998) 351/9111 (1286). , XP001105350 paragraph '0001!</p> <p>---</p>	1,2,21, 45,54
X	<p>SETHI G.R. ET AL: "Bronchiectasis: Causes and management." INDIAN JOURNAL OF PEDIATRICS, (2000) 67/2 (133-139). , XP001105351 abstract page 137, 'Role of Antibiotics'</p> <p>---</p>	1,2,21, 43,45, 54,55
X	<p>WALES D. ET AL: "The anti-inflammatory effects of macrolides." THORAX, (1999) 54/SUPPL. 2 (S58-S62). , XP001104995 page 559, right-hand column; table 1 page 560, left-hand column, paragraph 2 table 3 page 560, right-hand column, line 45-47 page 561, right-hand column, line 13 - line 18 page 561, right-hand column, line 25 - line 29 'Learning Point' 2</p> <p>---</p>	1,2,21, 45,54
X	<p>SPENCER D.: "Macrolide antibiotics in diffuse panbronchiolitis and in cystic fibrosis '2!'" EUROPEAN RESPIRATORY JOURNAL, (1998) 11/6 (1428). , XP001104988 the whole document</p> <p>---</p>	1,2,21, 45,54
X	<p>DESTACHE CHRISTOPHER J ET AL: "Clinical and economic considerations in the treatment of acute exacerbations of chronic bronchitis." JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY, vol. 43, no. SUPPL. 1, March 1999 (1999-03), pages 107-113, XP001104994 ISSN: 0305-7453 abstract 'Discussion', first and last paragraph</p> <p>---</p> <p>-/--</p>	1,2,21, 45,54

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/03984

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	FERNANDEZ-OBREGON, A. C.: "Azithromycin for the treatment of acne" INT.J. DERMATOL., vol. 39, 2000, pages 45-50, XP002213964 abstract page 45, left-hand column, line 10 - line 13 page 46, left-hand column, line 16 - line 17; table 2 page 46, right-hand column, line 17 - line 22 page 47, right-hand column, line 9 - line 11 'Discussion'	1, 3, 21-25, 45, 54
X	WO 99 24036 A (ORMEROD ANTHONY DAVID ; UNIV ABERDEEN (GB); WINFIELD ARTHUR (GB)) 20 May 1999 (1999-05-20) claims 3, 7, 8	1, 3, 21, 45, 54
X	DATABASE EMBASE 'Online! ELSEVIER SCIENCE PUBLISHERS, AMSTERDAM, NL; MOMIN A. ET AL: "Reiter's syndrome - 3 case report." retrieved from STN Database accession no. 1998054754 XP002213966 abstract & BANGLADESH JOURNAL OF DERMATOLOGY, VENEREOLOGY AND LEPROLOGY, (1997) 14/2 (49-53).	1, 3, 21, 45, 54
X	O'DELL J.R.: "Is there a role for antibiotics in the treatment of patients with rheumatoid arthritis?" DRUGS, (1999) 57/3 (279-282). , XP001104987 '4. Other Antimicrobials'	1, 4, 6, 21, 45, 54
X	GUI G. P. H. ET AL: "Two-year-outcomes analysis of Crohn's disease treated with rifabutin and macrolide antibiotics" JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY, (1997), 39(3), 393-400, 47 REFS. ISSN: 0305-7453 CODEN: JACHDX, XP001104989 University Department of Surgery, St George's Hospital Medical School, Cranmer Terrace, London SW17 0RE, United Kingdom abstract page 394, right-hand column, paragraph 1 page 398, left-hand column, line 13 - line 15	1, 4, 5, 21-26, 43-45, 54-56

-/--

INTERNATIONAL SEARCH REPORT

International Application No

PCT/EP 02/03984

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 00 25756 A (OTTERBECK NORBERT ;KIST MANFRED (DE); FALK PHARMA GMBH (DE)) 11 May 2000 (2000-05-11) abstract page 3, paragraph 2 page 5, paragraph 3 page 6, paragraph 2 -page 7, paragraph 1 page 9, paragraph 5 -page 10, paragraph 1 page 13, table claims 1,8,9,17-20,28,29,32,40-42	1,4,5, 7-33, 45-54
X A	EP 0 445 743 A (PLIVA PHARM & CHEM WORKS) 11 September 1991 (1991-09-11) page 2, line 21 - line 23 page 2, line 30 - line 44 claims 2,3,5,8-10,16-23	45,48, 49,54 11-14
X A	EP 0 467 331 A (PLIVA PHARM & CHEM WORKS) 22 January 1992 (1992-01-22) page 3, line 2 page 6, line 22 - line 26	45,46,54 7
X A	WO 01 00640 A (LUDESCHER JOHANNES ;GARCIA RAFAEL (ES); BIOCHEMIE SA (ES); DIAGO J) 4 January 2001 (2001-01-04) page 1, line 1 page 6, line 13 page 7, line 13,14,29,30 page 8, line 27 - line 30 page 11, line 9 - line 15	45,47, 51-54 9,10, 16-20
X A	WO 95 09601 A (PROCTER & GAMBLE) 13 April 1995 (1995-04-13) page 4, line 14 - line 16	45,51-54 16-20

INTERNATIONAL SEARCH REPORT

national application No.
PCT/EP 02/03984

Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this International application, as follows:

see additional sheet

1. ☐ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☒ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☐ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 2; 1 and 7-58 (partly)

Use of a pharmaceutical composition comprising azithromycin or derivatives thereof for the manufacture of a medicament for the treatment of neutrophil-dominated, non-infective inflammatory pulmonary disease.

2. Claims: 3; 1 and 7-58 (partly)

Use of a pharmaceutical composition comprising azithromycin or derivatives thereof for the manufacture of a medicament for the treatment of neutrophil-dominated, non-infective inflammatory skin disease.

3. Claims: 4, 6; 1 and 7-58 (partly)

Use of a pharmaceutical composition comprising azithromycin or derivatives thereof for the manufacture of a medicament for the treatment of neutrophil-dominated, non-infective inflammatory autoimmune disease.

4. Claims: 5; 1 and 7-58 (partly)

Use of a pharmaceutical composition comprising azithromycin or derivatives thereof for the manufacture of a medicament for the treatment of neutrophil-dominated, non-infective inflammatory intestinal disease.

INTERNATIONAL SEARCH REPORT

- information on patent family members

In International Application No

PCT/EP 02/03984

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
WO 9924036	A	20-05-1999	AU 1040899 A	31-05-1999
			BG 104370 A	29-12-2000
			BR 9815264 A	14-08-2001
			CA 2309159 A1	20-05-1999
			CN 1278173 T	27-12-2000
			EE 200000279 A	15-10-2001
			EP 1028727 A1	23-08-2000
			WO 9924036 A1	20-05-1999
			HR 20000233 A1	28-02-2001
			HU 0003675 A2	28-04-2001
			JP 2001522801 T	20-11-2001
			NO 20002078 A	06-07-2000
			PL 340710 A1	26-02-2001
			SK 6622000 A3	18-01-2001
			TR 200001238 T2	22-01-2001
			ZA 9810111 A	07-05-1999
WO 0025756	A	11-05-2000	DE 19850445 A1	04-05-2000
			WO 0025756 A2	11-05-2000
EP 0445743	A	11-09-1991	AT 143266 T	15-10-1996
			BG 61230 B1	31-03-1997
			CA 2037663 A1	08-09-1991
			CN 1054534 A ,B	18-09-1991
			CN 1054714 A	25-09-1991
			CN 1168891 A ,B	31-12-1997
			CS 9100587 A2	15-10-1991
			DE 69122282 D1	31-10-1996
			DK 445743 T3	17-02-1997
			EP 0445743 A2	11-09-1991
			ES 2094763 T3	01-02-1997
			GR 3021947 T3	31-03-1997
			HR 940256 A1	30-06-1997
			HU 56849 A2	28-10-1991
			HU 9500704 A3	28-11-1995
			JP 2731636 B2	25-03-1998
			JP 6184186 A	05-07-1994
			PL 166279 B1	28-04-1995
			RO 107660 B1	30-12-1993
			SI 9010455 A ,B	31-08-1997
			SK 279278 B6	09-09-1998
			RU 2039060 C1	09-07-1995
			RU 2039061 C1	09-07-1995
			US 5498699 A	12-03-1996
EP 0467331	A	22-01-1992	AT 129715 T	15-11-1995
			BG 60593 B1	29-09-1995
			CA 2046956 A1	19-01-1992
			CN 1059728 A ,B	25-03-1992
			CS 9102195 A3	18-03-1992
			DE 69114198 D1	07-12-1995
			DE 69114198 T2	27-06-1996
			DK 467331 T3	05-02-1996
			EP 0467331 A1	22-01-1992
			ES 2081397 T3	01-03-1996
			GR 3018330 T3	31-03-1996
			HR 920491 A1	31-08-1994
			HU 59935 A2	28-07-1992

INTERNATIONAL SEARCH REPORT

Information on patent family members

International Application No

PCT/EP 02/03984

Patent document cited in search report		Publication date	Patent family member(s)	Publication date
EP 0467331	A		HU 215158 B	28-12-1998
			HU 9500748 A3	28-12-1995
			JP 2657132 B2	24-09-1997
			JP 5132497 A	28-05-1993
			PL 291130 A1	16-11-1992
			RO 109338 B1	30-01-1995
			SI 9011409 A	31-10-1995
			SK 279075 B6	03-06-1998
			RU 2045533 C1	10-10-1995
			US 5250518 A	05-10-1993
WO 0100640	A	04-01-2001	AU 5820400 A	31-01-2001
			WO 0100640 A1	04-01-2001
			EP 1189915 A1	27-03-2002
WO 9509601	A	13-04-1995	AU 7957994 A	01-05-1995
			CA 2173109 A1	13-04-1995
			EP 0721324 A1	17-07-1996
			JP 9503504 T	08-04-1997
			WO 9509601 A1	13-04-1995